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Correlation between Haemorrhagic Complications and CT Findings before and after Intra-arterial Reperfusion Therapy for Acute Middle Cerebral Artery Occlusion

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Summary

The purpose of this study was to investigate whether haemorrhagic complications can be predicted by evaluating CT findings before and after intra-arterial reperfusion therapy for acute middle cerebral artery (MCA) occlusion. Pre-therapeutic early CT signs within three hours after onset and post-therapeutic contrast extravasation were evaluated in 61 patients treated within six hours after onset. Early CT signs were evaluated in the deep (obscuration of the margin of the lentiform nucleus and loss of the insular ribbon) and superficial MCA territories (cortical effacement). Haemorrhagic transformations were seen in 39.3% of patients, 54.2% of them had both pre-therapeutic early CT signs and post-therapeutic contrast extravasation. Obscuration of the entire lentiform nucleus and the presence of contrast extravasation were reliable predictors for haemorrhagic transformations, and cortical effacement had also a tendency to be associated with haemorrhage. Absence of early CT signs did not always result in the absence of haemorrhagic transformations and 37.5% of haemorrhage occurred in the presumed normal area without early CT signs. On the other hand, absence of post-therapeutic contrast extravasation was a reliable negative predictor for intraparenchymal haematoma.

Introduction

Prediction of haemorrhagic complications is the most important issue when deciding whether to perform reperfusion therapy [1]. The presence of pre-therapeutic early CT signs has been reported to be a reliable predictor for haemorrhagic complications [1,2]. To be sure, the incidence of haemorrhagic complications is significantly higher in patients with early CT signs [1]. In patients with MCA occlusion, however, the positive rate of parenchymal early CT signs may be fairly high, even within three hours after symptom onset [2] and early CT signs do not always result in haemorrhagic complications after reperfusion therapy. It is not well known which type of early CT signs are associated with blood-brain barrier (BBB) disruption and have risk for haemorrhage.

On the other hand, contrast extravasation on post-therapeutic CT, which reflects some degree of BBB disruption, has been reported to be a useful finding to predict the occurrence of haemorrhagic complications [3].

On the basis of these considerations, we investigated the incidence and clinical significance of pre-therapeutic early CT signs and post-therapeutic contrast extravasation in patients with angiographically proved MCA occlusions.

Methods

Since 1993, 61 MCA occluded patients underwent initial CT scanning within three hours after symptom onset and were treated with intra-arterial reperfusion therapies within six hours after symptom onset. There were 34 men and 27 women, 47 to 87 years old, with a mean age of 70.2 ± 9.8 years. Early CT signs were defined according to the following characteristics: obscuration of the margin of the lentiform nucleus, loss of the insular ribbon and cortical effacement [1,2]. Early CT signs in the deep MCA territories were graded into the following three grades according to their anatomic extent: grade I, normal basal ganglia with subtle hypodensity localized to the insula; grade II, partial obscuration of the postero-lateral part of the putamen; grade III, hypodensity of the entire lentiform nucleus [2]. Before the initiation of reperfusion therapy, a microcatheter was introduced beyond the thrombus and local angiography was performed to assess the size of thrombus or the precise site of occlusion. Therefore, contrast medium may be injected to the ischemic core even without recanalization. As for reperfusion therapy, either intra-arterial thrombolysis or direct percutaneous transluminal angioplasty (PTA) was performed. When early CT signs were present and/or lenticulostriate arteries were involved in ischemia, we preferred direct PTA to thrombolytic therapy as the first choice of the treatment [4,5]. Intra-arterial thrombolysis was performed using urokinase, native tissue plasminogen activator (t-PA) or both. Doses of urokinase ranged from 60,000 to 600,000 units, with 10 ml of saline per 60,000 units, in boluses. Doses of native t-PA ranged from 3.6 to 14.4 mg, with 10 ml of saline per 1.8 mg, in boluses. Direct PTA was performed with Stealth angioplasty balloon catheter with a maximum diameter of 2.0 to 2.5 mm. The balloon catheter was advanced into the occlusion site and inflated to 2 atm initially and subsequently up to 3 atm. Several inflations of 30 seconds each were performed until recanalization of the MCA trunk was established. To assess the presence of contrast extravasation, all patients underwent CT scanning immediately after the completion or discontinuance of reperfusion therapy [3]. Follow-up CT scans were obtained on the next day (about 24 hours later) and again three to seven days after the termination of the reperfusion therapy. Intraparenchymal hyperdense areas were defined as haemorrhages when they did not resolve until > 24 hours later [3]. Haemorrhagic transformations were subdivided into three types:

1) petechial haemorrhage with spotty and scattered hyperdense areas;

2) small haematoma with a homogenous hyperdense area < 3 cm in diameter;

3) massive haematoma with neurological worsening [1].

When hyperdense areas disappeared by the next day, they were considered to be only contrast extravasation [3]. We investigated correlation between haemorrhagic complications and CT findings before and after intra-arterial reperfusion therapy. Statistical analyses were performed using univariate tests (Mann-Whitney U and Kruskal-Wallis tests) and a logistic regression analysis. We chose a value of $p = 0.05$ as a level of statistical significance.

Results

Relationship between haemorrhagic transformations and CT findings before and after reperfusion therapy are shown in table 1. No fewer than 49 of the 61 patients (80.3%) had some early CT signs in the deep or superficial MCA territories. Forty-two of the 61 patients (68.9%) had early CT signs in the deep MCA territories, whereas only 17 (27.9%) had cortical effacement. There was a significant difference in the incidence of early CT signs between the deep and superficial MCA territories (Mann-Whitney U test, $p < 0.0001$). However, the incidences of post-therapeutic contrast extravasation in these two territories were not different (41.0% in the deep MCA territory and 42.6% in the cerebral cortex).

The presence of grade I or II signs had no significant influence to the incidence of haemorrhagic transformations ($p = 0.78$). However, grade III CT signs had significantly higher risk for the development of haemorrhagic transformations compared with the other two grades of early CT signs (OR, 19.80, 95% CI, 1.71 to 229.70). Cortical effacement also tended to develop into haemorrhagic transformations, though statistically significant risk was not proved ($p = 0.10$).

In 23 of the 42 (54.8%) patients with early CT signs in the deep MCA territories, post-

therapeutic contrast extravasation was seen in the corresponding areas of the pre-therapeutic early CT signs. On the other hand, 14 of the 17 (82.4%) cortical effacements were associated with contrast extravasation after intra-arterial reperfusion therapy. There were significant correlations between pre-therapeutic early CT signs and post-therapeutic contrast extravasation in both the deep and superficial MCA territories (Mann-Whitney U test, $p < 0.01$). Compared with early CT signs in the deep MCA territories, cortical effacement had an increased risk of association of contrast extravasation after intra-arterial reperfusion therapy (OR, 6.33, 95% CI, 1.87 to 21.40). Forty-three of the 61 patients (70.5%) had post-therapeutic hyperdense areas indicative of contrast extravasation or haemorrhage, 24 of them (55.8%) were associated with some types of haemorrhage and the other had only contrast extravasation. After all, 24 of the 61 patients (39.3%) had some types of haemorrhagic transformations, 13 of them (54.2%) had both pre-therapeutic early CT signs and post-therapeutic contrast extravasation. In both the deep and superficial MCA territories, absence of early CT signs did not always result in the absence of haemorrhagic transformations and more than one-third (37.5%) of haemorrhagic transformations occurred in the presumed normal areas without early CT signs. On the other hand, haemorrhagic transformations except for petechial haemorrhage never occurred in the areas without contrast extravasation.

Discussion

The incidence of early CT signs in the deep MCA territories was significantly higher than that in the cerebral cortex when early CT signs evaluation was restricted to the CT images obtained within three hours after symptom onset. However, our present study demonstrated that there were no significant differences in the incidences of post-therapeutic contrast extravasation and haemorrhagic transformations between the deep and superficial MCA territories, suggesting that ischemic damage may proceed similarly in these two territories. The lower detection rate of early CT signs in the cerebral cortex may be due to oversight of subtle early CT signs in the early stage of ischemia. Effacement of cortical sulci may be an advanced sign, which may be a result of extracellular vasogenic oedema associated with some injury to the endothelial cell permeability barrier. To be sure, 82.4% of cortical effacement was associated with post-therapeutic contrast

Table 1 **Relationship between haemorrhagic transformations and CT findings before and after reperfusion therapy**

Early CT signs or Ex	No.	Ex(+)	*Haemorrhagic transformations*			
			Massive	Small	Petechial	Total
Deep MCA territory						
Grade I	16	8 (50.0%)	0	2	0	2 (12.5%)
Grade II	22	13 (59.1%)	1	2	0	3 (13.6%)
Grade III	4	2 (50.0%)	1	1	1	3 (75.0%)*
Early CT (-)	19	2 (10.5%)	2	0	1	3 (15.8%)
Ex (+)		25 (41.0%)	4	5	0	9 (36.0%)*
Ex (-)		36 (59.0%)	0	0	2	2 (5.6%)
Superficial MCA territory						
Cortical effacement	17	14 (82.4%)	2	1	3	6 (35.3%)
Early CT (-)	44	12 (27.3%)	3	4	0	7 (15.9%)
Ex (+)		26 (42.6%)	5	5	3	13 (50.0%)*
Ex (-)		35 (57.4%)	0	0	0	0 (0%)

Ex; post-therapeutic contrast extravasation
**p<0.01, Mann-Whitney U or Kruskal-Wallis test*

extravasation in the corresponding area. Therefore, the presence of cortical effacement may be a reliable predictor for some degree of the endothelial damage and haemorrhagic transformations.

On the other hand, early CT signs in the deep MCA territories can be recognized from the early stage of ischemia without endothelial damage [2], which may result in the absence of contrast staining of the early CT signs. In our study, about half of the early CT signs in the deep MCA territories had no contrast staining. As the result, the incidence of haemorrhagic transformations in the deep MCA territories were only 15% or so regardless of the presence or absence of grade I or II CT signs, suggesting that the presence of grade I or II CT signs may not always be contraindication for intra-arterial reperfusion therapy. However, the presence of grade III CT signs may be a significant risk factor for haemorrhagic transformations.

Post-therapeutic CT just after reperfusion therapy was also useful in predicting haemorrhagic transformations [3]. Since contrast extravasation is the result of some injury to microvascular permeability and integrity, post-therapeutic contrast extravasation was a reliable predictor for haemorrhagic transformations. Furthermore, when contrast extravasation is not seen on the post-therapeutic CT just after intra-arterial reperfusion therapy, there may be little or no possibility of intraparenchymal haematoma.

Conclusions

Grade III CT signs and post-therapeutic contrast extravasation were reliable predictive signs for haemorrhagic transformations, and cortical effacement had also a tendency to be associated with haemorrhage. Absence of early CT signs was not always a negative predictor for haemorrhagic transformations, whereas absence of post-therapeutic contrast extravasation was a reliable negative predictor for intraparenchymal haematoma.

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